IN THE CLAIMS:

Please amend claims set forth below.

1. (Original) A method of inhibiting a ubiquitin isopeptidase in a cell, comprising contacting said cell with an effective amount of a composition comprising a compound having an α,β,-unsaturated ketone, wherein said ketone has a sterically accessible electrophilic β-carbon, wherein said agent is cell permeable and active in intact cells, and wherein said agent is not a cyclopentenane prostaglandin of the J family.

2. (Currently amended) The method according to claim 1, wherein said compound contains a cross-conjugated α,β, ~~α,β'~~ α',β' -unsaturated ketone moiety, and wherein at least one of said electrophilic β carbons is sterically accessible.

3. (Original) The method according to claim 2, wherein both of said electrophilic β carbons are sterically accessible.

4. (Currently amended) The method according to claim 2 ~~any preceding claim~~, wherein the α carbon of at least one α,β-unsaturated ketone moiety bears an electron withdrawing substituent.

5. (Original) The method according to claim 4, wherein said electron withdrawing substituent is selected from the group consisting of fluorine, chlorine, bromine, iodine, nitro, nitrilo and carboxy.

6. (Original) The method according to claim 5, wherein said carboxy group is an acid, ester of amide group.

7. (Currently amended) The method according to claim 1 ~~any preceding claim~~, wherein said α,β-unsaturated ketone comprises a conjugated cyclopentene moiety.

8. (Original) The method according to claim 1, wherein said compound is selected from the group consisting of dibenzylideneacetone (DBA), curcumin, shikoccin (NSC-302979), shikoccin epoxide, O-methyl shikoccin, O-methyl shikoccin epoxide, shikodomedin, rabdoshikoccin A, rabdoshikoccin B, rabdolatifolin, rabdoumbrasanin, and a punaglandin.

9. (Original) The method according to claim 8, wherein said compound is a punaglandin selected from the group consisting of PNG 2, PNG3, PNG4, Z-PNG4, and PNG 6.

10. (Original) A method of treating or alleviating an oncological malady in a subject, comprising administering to said subject a composition comprising an effective amount of a ubiquitin isopeptidase inhibitor.

11. (Currently amended) ~~A~~ The method according to claim 10, wherein said inhibitor comprises an α,β,-unsaturated ketone group having a sterically accessible electrophilic β-carbon, wherein said inhinitor is cell permeable and active in intact cells, and wherein said inhibitor is not a cyclopentenone prostaglandin of the J family..

12. (Currently amended) The method according to claim 11, wherein said ~~compound~~ inhibitor contains a cross-conjugated α,β, α',β', -unsaturated ketone moiety, and wherein at least one of said electrophilic, β carbons is sterically accessible.

13. (Original) The method according to claim 12, wherein both of said electrophilic β carbons are sterically accessible.

14. (Currently amended) The method according to claim 12 ~~any of claims 11-13~~, wherein the α carbon of at least one α,β-unsaturated ketone moiety bears an electron withdrawing substituent.

15. (Original) The method according to claim 14, wherein said electron withdrawing substituent is selected from the group consisting of fluorine, chlorine, bromine, iodine, nitro, nitrilo and carboxy groups.

16. (Original) The method according to claim 15, wherein said carboxy group is an acid, ester of amide group.

17. (Currently amended) The method according to claim 11 ~~any of claims 11-16~~, wherein said α,β-unsaturated ketone comprises a conjugated cyclopentene moiety.

18. (Original) The method according to claim 11, wherein said compound is selected from the group consisting of dibenzylideneacetone (DBA), curcumin, shikoccin (NSC-302979), shikoccin epoxide, O-methyl shikoccin, O-methyl shikoccin epoxide, shikodomedin, rabdoshikoccin A, rabdoshikoccin B, rabdolatifolin, rabdoumbrasanin, and a punaglandin.

19. (Original) The method according to claim 18, wherein said compound is a punaglandin selected from the group consisting of PNG 2, PNG3, PNG4, Z-PNG4, and PNG 6.

20. (Currently amended) The method according to claim 1 ~~any of claims 1-9~~ wherein said cell is a human cell.

21. (Currently amended) The method according to claim 10 ~~any of claims 10-19~~, wherein said subject is a human.

22. (Original) The method according to claim 10, wherein said oncological malady is selected from the group consisting of tumors of the head and neck, esophagus, stomach, ileum, colon, rectum, breast, ovary, prostate, testes, lung, brain, kidney, liver, pancrease, muscle (sarcoma), connective tissue (sarcoma) or fat (sarcoma), bone marrow, lymphomas and leukemias.

23. (Original) A pharmaceutical composition suitable for treating an oncological malady in a human subject, comprising an effective amount of a ubiquitin isopeptidase inhibitor, wherein said inhibitor is not a cyclopentenone prostaglandin of the J family.

24. (Original) The composition according to claim 23, wherein said inhibitor comprises an α,β-unsaturated ketone moiety, wherein said ketone has a sterically accessible electrophilic β-carbon, wherein said agent is cell permeable and active in intact cells, and wherein said agent is not a cyclopentenone prostaglandin of the J family, together with a pharmaceutically acceptable carrier, excipient, or diluent.

25. (Currently amended) The method according to claim 10 ~~any of claims 10-22~~, wherein said composition further comprises an effective amount of at least one additional pharmaceutically active antineoplastic agent.

26. (Original) The method according to claim 25, wherein said additional antineoplastic agent is selected from the group consisting of a topoisomerase 2 inhibitor, a DNA methyltransferase inhibitor, a topoisomerase 1 inhibitor, and a cyclopentenone prostaglandin of the J series.

27. (Currently amended) ~~A~~ The method according to claim 26, wherein said additional agent is selected from the group consisting of etoposide, decitibine, and an active camptothecin analog.

28-35 (Canceled)

36. (New) A method of treating a disorder mediated by a proteosome pathway in a patient, comprising administering to said patient an effective amount of a ubiquitin isopeptidase inhibitor, wherein said disorder is selected from the group consisting of, dry eye disorder, restenosis, inflammation, autoimmune disorder, graft rejection, ischemia, cachexia, muscle wasting and loss of bone or hair.

37. (New) The method according to claim 36, wherein the disorder is dry eye disorder.

38. (New) The method according to claim 36, wherein the disorder is restenosis.

39. (New) The method according to claim 36, wherein the disorder is inflammation.

40. (New) The method according to claim 36, wherein the disorder is an autoimmune disorder.

41. (New) The method according to claim 36, wherein the disorder is graft rejection.

42. (New) The method according to claim 36, wherein the disorder is ischemia.

43. (New) The method according to claim 36, wherein the disorder is cachexia.

44. (New) The method according to claim 36, wherein the disorder is muscle wasting.

45. (New) The method according to claim 36, wherein the disorder is a loss of bone or hair.